

REMARKS

The Office Action dated February 22, 2005, has been received and reviewed. Claims 1, 4-7, 10, 13-18, 21, 24-29 and 33-36 are pending in the present application. Claims 1, 4-7, 10, 13-18, 21, 24-29 and 33-36 stand rejected. Applicants have amended the priority claim to recite to the U.S. Patent Number and correct provisional number. Applicants have also amended the title of the invention as requested by the Examiner. Applicants have also amended the specification to correct for typographical errors in the parent application, particularly those in Tables 1-4. Applicants respectfully request reconsideration of the application as amended herein and in view of the arguments below.

I. Claim Amendments

Claims 6, 15, 18, 26 and 29 have been amended to further clarify the invention. Accordingly, Applicants respectfully request reconsideration of the application.

II. Double Patenting

Claims 1, 4-7, 10, 13-18, 21, 24-29 and 32 stand rejected under the judicially created doctrine of obviousness-type double patentable as being unpatentable over Claims 1-21 of U.S. Patent No. 6,844,334. Applicants appreciate the fact that the Office Action notes that the conflicting claims are not identical to one another. In an effort to expedite prosecution of the present application, Applicants have included a terminal disclaimer for Claims 1-21 of U.S. Patent No. 6,844,334.

Claims 1, 4-7, 10, 13-18, 21, 24-29 and 32 stand rejected under the judicially created doctrine of obviousness-type double patentable as being unpatentable over Claims 1-21 of U.S. Patent No. 6,660,726. Applicants appreciate the fact that the Office Action notes that the conflicting claims are not identical to one another. In an effort to expedite prosecution of the present application, Applicants have included a terminal disclaimer for Claims 1-21 of U.S. Patent No. 6,660,726.

Claims 10, 13-18, 21, 24-29 and 32 also stand rejected under the judicially created doctrine of obviousness-type double patentable as being unpatentable over Claims 1-21 of U.S. Patent No. 6,855,703. Again, Applicants appreciate the fact that the Office Action notes that the conflicting claims are not identical to one another. In an effort to expedite

prosecution of the present application, Applicants have included a terminal disclaimer for Claims 1-21 of U.S. Patent No. 6,855,703.

Claims 35 and 36 stand objected to as allegedly being a substantial duplicate of Claims 33 and 34. Applicants respectfully disagree with this assertion. Applicants note that the claims may be differentiated as at position C(17) there is either a hydroxyl or an oxygen. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to these claims.

III. Claim rejections 35 U.S.C. § 112, first paragraph

Claims 18 and 29 stand rejected as allegedly the term "derivatives" lacks description in the specification. Applicants note that the term "derivatives" does not lack description in the specification. At page 9, lines 1-2, the specification states "vitamin D and its derivatives (e.g., calcitriol and mixtures and blends thereof)." (Emphasis added). Applicants respectfully submit that, in view of the specification, one skilled in the art would readily understand that the recitation "vitamin D and its derivatives" means vitamin D and derivatives of vitamin D having substantially the same biological activity as vitamin D. Moreover, this is consistent with the use of the phrase in other U.S. Patents. For example, U.S. Patent 5,990,098 discloses "vitamin D or derivatives thereof." However, in an effort to expedite this application toward allowance, Applicants have amended these claims to remove "and its derivatives". Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, second paragraph rejections to Claims 18 and 29.

Claims 33-36 stand rejected as allegedly not being taught by the present application. Applicants respectfully disagree with this assertion. Applicants note page 3, lines 1-4 illustrate these compounds and glucuronides. Furthermore, the figures in the application illustrate the specific peaks in the ¹H-NMR spectrum and ¹³C-NMR spectrum. Accordingly, Applicants submit that they were in possession of the claimed invention at the time of filing. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections to Claims 33-36.

IV. 35 U.S.C. § 112, second paragraph

Claims 1, 4-7, 10, 13-18, 21, 24-29 and 32 also stand rejected under 35 U.S.C. § 112 as allegedly it is unclear how R₄-R₇ or R₁₀-R₁₃ can represent a ketone. Applicants submit that it is at this position where a ketone is formed, not at the carbon that the R₄-R₇ or R₁₀-R₁₃ is

attached. Accordingly, Applicants request reconsideration and withdrawal of the rejections to Claims 1, 4-7, 10, 13-18, 21, 24-29 and 32.

Claims 6, 15 and 26 have been further rejected under 35 U.S.C. § 112 as allegedly it is not clear how the compound can have a \exists orientation. Applicants note that it is possible for the rings to tautomerize and leave one of the positions in which all the double bonds are not in conjugation. Therefore, it is possible to have both an \forall and a \exists orientation. Applicants have amended Claims 6, 15 and 26 to note the specific orientation at the C(17) position. Accordingly, Applicants request reconsideration and withdrawal of the rejections to Claims 6, 15 and 26.

V. 35 U.S.C. § 102, anticipation rejections

Claims 1, 4-7, 10, 13-16, 21, 24-27 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Harnik (IL 25265). Applicants respectfully traverse this rejection as set forth below.

Case law holds and the M.P.E.P. states that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Additionally, anticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention. *Apple Computer Inc. v. Articulate Systems Inc.* 57 USPQ2d 1057, 1061 (Fed. Cir. 2000).

Applicants submit that Harnik does not anticipate the present invention for at least the following reasons. Independent Claims 1 and 10 recite "R₃ is hydrogen, sulfate, glucuronide or a conjugate thereof." In contrast, Harnik proposes compounds having a methoxy group at the 3 position of a 1,3,5,6,8 estrapentaene backbone. Harnik neither discloses nor suggests the claimed compounds having the recited substituents at the 3 position. Applicants further note that Claim 1 further recites that the compounds of Claim 1 "are present in chemically pure form." All of Harnik's proposed compounds appear to be present as reaction product mixtures. Harnik does not disclose or suggest compounds present in chemically pure form as recited in Claim 1. Thus, Harnik does not disclose, either explicitly or inherently, each and every element of the claims. Claim 10 is also not anticipated by Harnik for as Claim 10

recites, in part, "A pharmaceutical composition incorporating a compound represented by Formula I." Harnik proposes synthesis of particular estrogenic estrane derivatives. Harnik neither discloses nor suggests a pharmaceutical composition incorporating a compound represented by Formula I as recited in Claim 10. Applicants also note that independent Claim 21 and its dependent claims are not anticipated by Harnik for reasons similar to those provided with respect to Claim 1 above. Additionally, Claim 21 recites, in part, "A method of treating mammals in need of treatment for conditions treatable by estrogen therapy, said method comprising administering an effective amount of a compound represented by Formula I." Harnik proposes synthesis of particular estrogenic estrane derivatives. Harnik neither discloses nor suggests a method of treating mammals in need of treatment for conditions treatable by estrogen therapy, which method comprises administering an effective amount of a compound represented by Formula I as recited in Claim 21.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections to Claims 1, 4-7, 10, 13-16, 21 and 24-27.

VI. 35 U.S.C. § 103(a), obviousness type rejections

Claims 17-18 and 28-29 and 32 stand rejected under 35 U.S.C. § 103(a) over Harnik. It is alleged that it would have been obvious to combine two or more compounds having the same use to form a third use, thus it would allegedly be obvious to combine another estrogenic compound with the compounds of Harnik with the expectation that the combination would maintain its estrogenic property and be useful in treatment of hypo estrogenic conditions known in the art such as those associated with menopause. Applicants respectfully disagree with this assessment.

To establish a *prima facie* case of obviousness, the prior art reference or references when combined or modified must teach or suggest *all* the recitations of the claim, and there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). To support combining references, evidence of a suggestion, teaching, or motivation to combine must be **clear and particular**, and this

requirement for clear and particular evidence is not met by broad and conclusory statements about the teachings of references. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Court of Appeals for the Federal Circuit has also stated that, to support combining or modifying references, there must be **particular** evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, **would have selected these components for combination in the manner claimed**. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Respectfully, as will be discussed below, the Official Action fails to meet the requirements for a showing of obviousness under § 103.

Applicants note that Harnik fails to disclose the elements of independent Claim 10 of which Claims 17-18 depend from. Accordingly, Claims 17 and 18 are allowable for the same reasons as Claim 10. Furthermore, Applicants note that Harnik fails to disclose the elements of independent Claim 21 of which Claims 28-29 and 32 depend from. Applicants note that independent Claim 21 recites that R_3 is selected from the group consisting of hydrogen, sulfate, and glucuronide or other esters. In Harnik this grouping is only disclosed as methoxy. Harnik neither teaches nor suggests such a replacement of the group as recited in independent Claim 21. Furthermore, Claims 28-29 and 32 are directed to methods of treatment. Harnik merely discloses estrogenic estrane derivatives and fails to disclose methods of treatment as suggested in the presently claimed invention. There is no motivation taught or suggested by Harnik that its set of compounds would be useful for estrogen therapy such as the present compounds. Accordingly, Applicants respectfully such that Claims 17-18, 28-29 and 32 are not obvious in view of Harnik and the withdrawal of the rejections to these claims is respectfully requested.

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CONCLUSION

In view of the remarks presented herein, Applicants respectfully submit that the claims define patentable subject matter. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

It is believed that no other fees and/or additional fee(s)-including fees for net addition of claims-are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that an extension of time is necessary to allow consideration of this paper, such an extension is hereby petitioned under 37 C.F.R. §1.136(a). Any additional fees believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully Submitted,

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